

Obtunding the sympathetic response to intubation

Experience at 2 minutes after administration of the test agent in patients with cerebral aneurysms

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Summary

The sympathetic response to laryngoscopy and intubation was studied in 39 patients who were to undergo surgical clipping of a cerebral aneurysm. Intravascular radial artery pressure and ECG monitoring for ST-segment changes or dysrhythmias were used. Ward blood pressures were controlled on bed rest and labetalol. Induction of anaesthesia was with pentothal 4 mg/kg and suxamethonium 1 mg/kg intravenously. This was followed by one of the following intravenous agents by random choice: alfentanil 30 µg/kg, fentanyl 5 µg/kg, lignocaine 2 mg/kg, and lignocaine 10% spray 2 mg/kg to the larynx.

ECG changes at laryngoscopy and intubation were minimal. Intubation produced an immediate increase in blood pressure and pulse rate, maximal at 30 - 60 seconds, falling rapidly towards normal within 2 - 3 minutes. Alfentanil was very effective in obtunding this response with stable cardiovascular parameters; fentanyl produced a more variable response; and intravenous lignocaine was less satisfactory. Lignocaine spray was ineffective.

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Intubation of the larynx results in catecholamine release¹ and a marked hypertensive and tachycardiac response, usually of short duration.^{1,2} In the cardiac-compromised patient^{2,3} or patient with weakened blood vessels, this response may prove fatal. A cerebral aneurysm is at particular risk of rupture at this time.^{4,5}

Numerous methods have been used to obtund this response, some having the danger of a post-intubation hypotension.^{5,6} In addition, the authors of many studies utilised automatic blood pressure measuring devices,^{5,7} now proven to be unreliable for individual readings.^{8,9}

It was therefore decided to use direct arterial line recordings to study control of this response in cerebral aneurysm patients. Four methods commonly used in our hospital were chosen — intravenous alfentanil,^{5,7} fentanyl^{5,7} and lignocaine^{10,11} and laryngeal lignocaine spray.^{6,11}

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Patients and methods

Thirty-nine patients scheduled for clipping of cerebral aneurysms after subarachnoid haemorrhage were studied. The study was approved by the Tygerberg Hospital Medical Ethics Committee and all patients gave informed consent. Known hypertensive patients or cardiac cases were excluded. All patients were on bed rest and daily oral labetalol 300 - 600 mg in divided doses as needed to control ward blood pressure to a systolic reading below 150 mmHg.

Patients were randomly allocated to one of four groups done on the morning list: group A — alfentanil 30 µg/kg intravenously, group B — fentanyl 5 µg/kg intravenously, group C — lignocaine 2 mg/kg intravenously, and group D — lignocaine 2 mg/kg via laryngeal spray using 10% lignocaine (control).

The afternoon before surgery, resting pulse and blood pressure were measured with a standard baumanometer. Premedication was oral diazepam 0,15 mg/kg 2 hours before anaesthesia plus the morning labetalol dose. A 20-gauge radial artery Teflon cannula was inserted under local analgesia, and the ECG was recorded from bipolar leads in the CM5 configuration. The arterial line used a Gould-Statham transducer type number P23.

The patient was pre-oxygenated and induced with pentothal 4 mg/kg and suxamethonium 1 mg/kg. After fasciculations, the test agent was administered and the patient ventilated for 2 minutes on nitrous oxide 4 l/min and oxygen 2 l/min to maintain a capnograph reading of 5%. Intubation utilised a McIntosh No. 3 bladed laryngoscope and an 8 mm or 9 mm armoured cuffed Ruschelite endotracheal tube, depending on the gender of the patient.

All intubations were done by the same anaesthetist (K.P.) and completed without difficulty. Anaesthesia was maintained at the same flow rates and capnograph reading with a Spiromat ventilator. Systolic and diastolic blood pressure and pulse rate readings were taken 5 minutes after placing all lines and before pre-oxygenation, the highest level achieved at laryngoscopy and intubation, and post-intubation at 3 minutes, 5 minutes and 10 minutes (Table II). ECG printouts were studied for changes in rhythm and ST segments.

Statistical analysis was done using the non-paired Student's *t*-test for comparing the means of normally distributed data and the Mann-Whitney ranked *U*-test for skewed data. Fisher's exact probability test was used to compare the lignocaine spray group with the other groups. A *P* value of < 0,05 (two-tailed) was considered significant.

Results

Treatment of group D was terminated after 5 patients all had systolic blood pressures peaking at over 200 mmHg. The mean ages and weights of the four groups are given in Table I. ECG ST depression, defined as more than 1 mm, occurred in 1 group C and 1 group D patient. It was transient in nature. No dysrhythmias were noted.

Laryngoscopy in all groups caused no change in pulse rate or blood pressure. Initial lignocaine spraying in group D caused minor increases of less than 10%. Intubation caused an increase in the mean pulse rate and blood pressure within seconds in all

TABLE I. AGES AND WEIGHTS (MEAN \pm SE) OF THE FOUR GROUPS

	Group A	Group B	Group C	Group D
No. of patients	12	12	12	5
Age (yrs)	33 \pm 3,4	36 \pm 3,7	34 \pm 4,1	49 \pm 3,0
Weight (kg)	65 \pm 1,7	69 \pm 3,9	60 \pm 2,8	67 \pm 10,0

Patients in group D were significantly older than those in groups B and C; $P < 0,05$. If the 5 oldest patients of groups A, B and C are taken, their respective mean ages are 47 \pm 3,2 years, 48 \pm 3,0 years and 46 \pm 3,7 years. The blood pressure responses of these subgroups were not different from the full group. Patients in group B were significantly heavier than those in group C; $P < 0,05$.

groups. This was maximal at 30 - 60 seconds and then rapidly returned towards normal within 2 - 3 minutes of intubation.

Table II gives the mean \pm SE and range of blood pressure and pulse rate recorded during the study. Fig. 1 is the mean systolic blood pressure. All groups had non-significant rises in systolic blood pressure from the resting ward level to the pre-induction level. Thereafter groups C and D had significant rises on intubation ($P < 0,05$). Intergroup comparisons show that alfentanil provides a significantly flatter response than intravenous lignocaine ($P < 0,02$) and lignocaine spray ($P < 0,01$). Using the ward level as a reference, group A had no significant change for the rest of the study period while group B had significant decreases at 5 and 10 minutes.

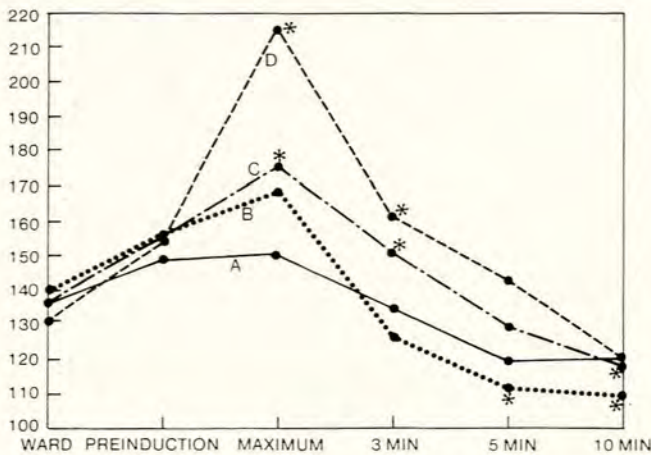


Fig. 1. Mean systolic blood pressure levels. Significant ($P < 0,05$) variations from ward levels are marked with an asterisk. Group A gave a significantly flatter response than group C ($P < 0,02$) and group D ($P < 0,01$).

Group A had the most stable blood pressure at intubation, only 2 patients had a systolic blood pressure raised by more than 20%, and none dropped by more than 20%. In group B 7 patients had an above 20% increase in systolic blood pressure, while in 2 patients it dropped by more than 20%. Group C produced 4 patients with a systolic blood pressure rise above 20% and 8 with rises of 0 - 2%, while all 5 patients in group D produced rises above 20%.

Fig. 2 shows the mean diastolic blood pressure. The pattern is similar to the systolic changes. Group A had a significantly flatter response than group C ($P < 0,05$) and group D ($P < 0,01$). Groups B and C obtunded the response better than group D ($P < 0,01$).

Fig. 3 shows mean pulse rate changes. From ward to theatre, no changes occurred. Thereafter all groups had a significant ($P < 0,05$) rise at intubation. Group A had significantly less rise than group C ($P < 0,02$). In groups A and B the rates at 3, 5 and 10 minutes were no different from ward or pre-intubation levels.

TABLE II. BLOOD PRESSURE AND PULSE RATES IN THE FOUR GROUPS (MEAN \pm SE AND RANGE)

Group	Ward			Pre-induction			Highest			3 min			5 min			10 min		
	Mean \pm SEM	Range		Mean \pm SEM	Range		Mean \pm SEM	Range		Mean \pm SEM	Range		Mean \pm SEM	Range		Mean \pm SEM	Range	
Systolic blood pressure (mmHg)																		
A	136 \pm 2,3	110 - 160		149 \pm 4,4	125 - 165		150 \pm 7,5	110 - 205		135 \pm 8,1	110 - 180		120 \pm 8,9	90 - 160		120 \pm 9,5	80 - 199	
B	140 \pm 5,0	130 - 150		156 \pm 2,8	142 - 170		168 \pm 14,7	112 - 240		126 \pm 10,4	91 - 180		111 \pm 5,7	90 - 157		109 \pm 4,1	90 - 133	
C	137 \pm 5,4	120 - 180		155 \pm 7,2	138 - 215		175 \pm 7,3	149 - 231		150 \pm 4,5	124 - 188		129 \pm 4,2	108 - 146		118 \pm 4,3	93 - 140	
D	132 \pm 9,6	110 - 160		154 \pm 4,9	142 - 170		215 \pm 4,5	204 - 230		161 \pm 8,7	137 - 185		142 \pm 7,7	128 - 169		120 \pm 3,2	108 - 126	
Diastolic blood pressure (mmHg)																		
A	75 \pm 2,6	50 - 80		75 \pm 2,4	62 - 86		82 \pm 4,6	58 - 110		73 \pm 4,2	60 - 100		62 \pm 4,4	50 - 88		64 \pm 4,4	51 - 93	
B	75 \pm 3,6	60 - 90		84 \pm 2,3	75 - 100		89 \pm 8,0	55 - 140		70 \pm 5,5	50 - 100		64 \pm 3,6	54 - 91		64 \pm 3,2	54 - 83	
C	74 \pm 2,9	70 - 100		75 \pm 4,6	64 - 110		97 \pm 4,6	84 - 128		82 \pm 2,6	69 - 99		70 \pm 3,9	55 - 81		67 \pm 3,7	49 - 77	
D	83 \pm 6,2	70 - 100		78 \pm 2,0	73 - 85		122 \pm 6,5	110 - 145		87 \pm 4,6	80 - 100		77 \pm 3,1	71 - 88		67 \pm 2,4	63 - 73	
Pulse rate (/min)																		
A	69 \pm 3,0	55 - 85		71 \pm 3,2	54 - 86		84 \pm 4,4	60 - 110		74 \pm 3,7	51 - 97		72 \pm 3,3	47 - 82		71 \pm 4,0	42 - 87	
B	72 \pm 2,1	60 - 82		74 \pm 4,9	53 - 103		88 \pm 5,4	55 - 112		76 \pm 5,0	51 - 102		77 \pm 4,9	50 - 108		76 \pm 4,6	50 - 108	
C	68 \pm 2,6	56 - 80		75 \pm 3,3	58 - 88		100 \pm 2,8	82 - 113		89 \pm 2,8	72 - 100		83 \pm 1,7	71 - 90		84 \pm 3,5	60 - 100	
D	72 \pm 4,0	60 - 80		70 \pm 4,0	65 - 80		101 \pm 8,6	70 - 115		84 \pm 5,1	65 - 90		80 \pm 4,2	78 - 90		75 \pm 2,8	65 - 81	

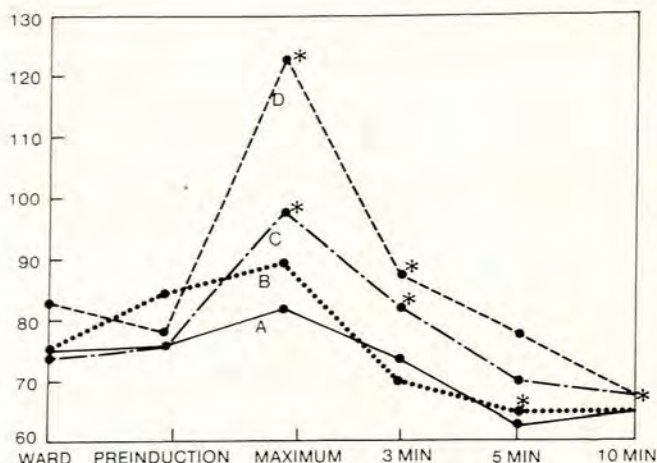


Fig. 2. Mean diastolic blood pressure levels. Significant ($P < 0,05$) variations from ward levels are marked with an asterisk. Group A gave a significantly flatter response than group C ($P < 0,05$) and group D ($P < 0,01$).

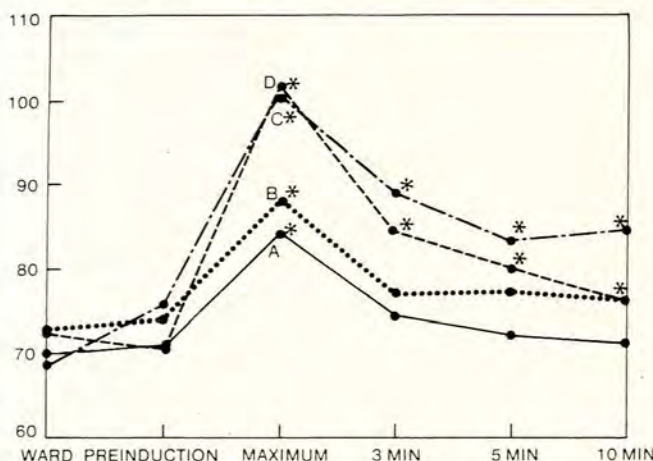


Fig. 3. Mean pulse rates. Significant ($P < 0,05$) variations from ward levels are marked with an asterisk.

Discussion

The cerebral circulation is protected from increases in systemic blood pressure below a mean of 130 mmHg by its inherent autoregulation.¹² Nevertheless, sudden sharp rises in systemic blood pressure do cause increases in intracranial pressure,^{11,13} hence rupture of a cerebral artery aneurysm is always a potential danger during intubation.^{4,5}

The danger of rupture of an aneurysm is related to the increased wall tension resulting from the raised transmural pressure, i.e. blood pressure minus intracranial pressure, peak tension being related to peak pressure. Utilising Laplace's law to calculate a mean increase in wall tension for these groups, gives values of 10% for alfentanil, 20% for fentanyl, 28% for intravenous lignocaine and 63% for lignocaine laryngeal spray. These mean values disguise the far greater variability in the effectiveness of fentanyl compared with alfentanil. This greater reliability of alfentanil is probably because of its speed of onset.¹⁴

Alfentanil is a more rapidly and less variably acting agent than fentanyl, peak action being at 1 - 2 minutes compared with 5 - 15 minutes.^{14,15} It is also one-quarter to one-third as potent an analgesic,^{14,15} but the same ratio does not necessarily apply to obtunding the intubation response.^{7,16} The choice of dose for this action has varied from 8 - 50 $\mu\text{g}/\text{kg}$.^{7,14,16} The doses of the four agents chosen and the time of administration have been reported as successful in patients free from neurological or cardiovascular disease.^{5-7,10,11} However, these studies utilised non-invasive methods of blood pressure measurement and are likely to have missed peak pressures.^{8,9}

As expected, since all patients were on labetalol therapy, pulse rate changes were less marked than in previous studies.² ECG changes have been noted at intubation.^{3,15} That they were not seen in this study is most probably because of the pre-oxygenation routine and because patients were on labetalol therapy.²

The lack of response to laryngoscopy is surprising in view of reports that it alone will trigger sympathetic stimulation.^{2,11} The brief duration of laryngoscopy would have contributed to this lack of response,^{6,17} as would the preparation of the patients with labetalol.²

We have shown that lignocaine 2 mg/kg intravenously or by rapid laryngeal spray does not protect patients from the transient but marked sympathetic response to intubation. Alfentanil 30 $\mu\text{g}/\text{kg}$ is effective in obtunding this response and gives a more reliable effect than fentanyl 5 $\mu\text{g}/\text{kg}$.

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